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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,946	03/15/2004	Shuang-yong Xu	NEB-183-CIP	2242
28986	7590	04/18/2006	EXAMINER	
HARRIET M. STRIMPEL; NEW ENGLAND BIOLABS, INC. 240 COUNTY ROAD IPSWICH, MA 01938-2723			PATTERSON, CHARLES L JR	
			ART UNIT	PAPER NUMBER

1652

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/800,946

Applicant(s)

XU ET AL.

Examiner

Charles L. Patterson, Jr.

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1652

The disclosure is objected to because of the following informalities:

On page 6, line 16, there is a "(" without a corresponding ")". This is confusing.

The recitation of "[e]xample 3 describes how a DNA linker...may be inserted between the coding region for a methylase and the coding region for the restriction endonuclease" is apparently incorrect. Example 3 describes various methylase deletions, not insertion of a linker.

On page 32, line 7, the recitation of "Figure 2" is apparently incorrect. Figure 2 shows the sequence of the *BpmI* methylase and the DNA encoding it. Perhaps the instant recitation should be "Figure 4".

The recitation on page 32, line 8 of "g type N6 adenine methylase" is not understood. Could applicant be referring to the λ type methylase as recited on page 28, line 20?

The recitation of "Figure 4" on line 19 of page 36 is apparently incorrect. Apparently the correct recitation is "Figure 7".

The meaning of the motifs in claims 3 and 5-6 is deemed "essential matter" and is perhaps referring to λ group in Figure 1C of Malone, et al. (AX). However, this material is not included in the instant specification and is essential to an understanding of what is being claimed. Applicants may add the necessary material to the instant specification as long as it is in some prior art publication, but it may not be incorporated by reference except to a U.S. Patent or a U.S. patent publication (37 CFR § 1.57(c)).

Similarly the sequences for the endonuclease and methylase of *AcuI*, *BsgI* and possibly *ThaIVp* are deemed essential matter. The sequences for *AcuI* and *BsgI* are essential to follow the genetic manipulations disclosed in the instant specification. If one wants to follow the disclosure of Example 7, apparently the sequences for *ThaIVp* are also essential.

Art Unit: 1652

Appropriate correction is required.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is confusing and indefinite in the recitation of "optionally" on line 10. It is not clear from the claim language what is to be "optionally" inactivated and when the option is to be exercised. Is the cleavage domain to be inactivated? Is the functional methylase domain and/or the specificity domain to be inactivated?

Claim 6 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot refer to another multiple dependent claim (claim 5). See MPEP § 608.01(n).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

On page 32, lines 7-10, it is stated that "in [t]he methylase domains of BpmI and AcuI...[m]otif IV...has a GNPPY sequence". The sequence of AcuI me-

Art Unit: 1652

thylase is not disclosed in the instant specification, but looking at the methylase sequence of *BpmI* (SEQ ID NO:2) a GNPPY sequence is not seen. The closest thing to that is at residues 120-124 there is a "Gly-Asn-Pro-Pro-Phe" sequence, i.e. GNPPF. On page 32, lines 13-16, the recitation of "D80A" and "Phe520" is not understood. Residue 80 in SEQ ID NO:4 is "Asn" while residue 520 is "Pro". Apparently the instant recitations are meant to refer to the *AcuI* sequence alone, which sequence is not included in the sequence disclosure of the instant application.

On page 34, lines 21-26, it is stated that "[a] chimeric enzyme was constructed between *BpmI* and *BsgI*, in which the N-terminal coding sequence (catalytic domain plus methylase motifs I to III) was derived from *BpmI* and the C-terminal coding sequence (methylase motifs IV to X and the specificity domain) was derived from *BsgI*". In Malone, et al. (AX), Figure 1C shows that the order of the gene for the methylase is "X-I-II-III-IV-V-VI-VI-VIII". Therefore it apparently is impossible for the N-terminal end to be the "catalytic domain plus methylase motifs I to III" since motif "X" is between the catalytic domain the motif I. Similarly, the C-terminal coding sequence being from "motifs IV to X" is apparently impossible since "X" is at N-terminal end of the motifs, before "I". This is not understood and apparently is impossible.

On page 35, lines 1-4 it is stated that the amino acid sequences in the fusion junctions are "FDAIIGNPPY" in *BpmI* and "FDVILPNPPY" in *BsgI*. The sequence for *BsgI* methylase is not given in the instant specification but the sequence "FDAIIGNPPY" is not seen in SEQ ID NO:2 for *BpmI*.

Apparently an altered restriction endonuclease prepared according to claims 11-16 is not disclosed in the specification. If applicants assert that it is disclosed, they should specifically point out where.

Art Unit: 1652

Finally, the instant specification appears to be enabling only for the *BpmI/BsgI* chimeric protein, the results of which are discussed on page 36, if it is enabled for anything. Apparently only this chimeric protein has been tested for cleavage alteration and therefore the instant claims should be so limited. One of ordinary skill in the art would not know what the chimeric enzymes of the instant claims would produce.

It is maintained that with the instant discrepancies, one of ordinary skill in the art could not practice the instant invention without undue experimentation.

It is stated for the record that apparently the instant claims do not have support under 35 USC § 112 in the parent application and therefore are entitled only to the filing date of the instant application.

Nelson, et al. (U) is cited as of interest in that it teaches a method of altering recognition specificities of restriction endonucleases with methylases. Samuelson, et al. (A) and Janulaitis, et al. (B) are cited as of interest, but it is deemed that the instant claims define over these references since the instant claims are limited to Type IIG enzymes and contain specific mutation methods different than the references.

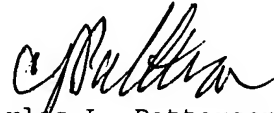
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 571-272-0936. The examiner can normally be reached on Monday - Friday from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on 571-272-

Art Unit: 1652

0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
April 4, 2006